

Claims

1. A method for in vitro expansion of mammalian stem or progenitor cells, the method comprising the steps of:
  - (a) providing an Asb-a polypeptide to the stem or progenitor cells whereby the  
5 intracellular concentration of the Asb-a polypeptide is sufficient to prevent differentiation of the cells; and,
  - (b) culturing the stem or progenitor cells for a period of time sufficient for the cells to divide and self-renew.
- 10 2. A method according to claim 1, whereby the intracellular concentration of the Asb-a polypeptide is maintained at a level sufficient to prevent differentiation of the cells for a period of time sufficient for the cells to divide and self-renew until the population of the stem or progenitor cells has reached a desired size.
- 15 3. A method according to claims 1 or 2, whereby the Asb-a polypeptide is provided to the cells by addition of an exogenous Asb-a polypeptide to the culture medium.
4. A method according to claim 3, whereby the Asb-a polypeptide is fused to a transport moiety.
- 20 5. A method according to claim 4, whereby the Asb-a polypeptide is genetically fused to a transport moiety.
6. A method according to claims 4 or 5, whereby the transport moiety is a fragment  
25 of an HIV tat protein.
7. A method according to claims 1 or 2, whereby the Asb-a polypeptide is provided to the cells by introducing an exogenous nucleic acid comprising a nucleotide sequence encoding the Asb-a polypeptide into the stem or progenitor cells.
- 30 8. A method according to claim 7, whereby the nucleic acid is an RNA molecule capable of being translated in the stem or progenitor cells.

9. A method according to claim 7, whereby the exogenous nucleic acid is an expression vector wherein the nucleotide sequence encoding the Asb-a polypeptide is operably linked to a promoter that is capable of regulating transcription in the stem or progenitor cells.
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10. A method according to claim 9, whereby the expression vector is a vector for transient expression of the nucleotide sequence encoding the Asb-a polypeptide.
11. A method according to claim 10, whereby the vector is an episomal vector that
- 10 does not replicate in the stem or progenitor cells.
12. A method according to claim 9, whereby the vector comprises sites for recombination flanking the nucleotide sequence encoding the Asb-a polypeptide.
- 15 13. A method according to claim 12, whereby the vector integrates in to the genome of the stem or progenitor cells.
14. A method according to claim 12, whereby the vector is a retroviral vector.
- 20 15. A method according to any one of claims 1 - 14, whereby the stem or progenitor cells are selected from the group consisting of hematopoietic stem cells, neural crest stem cells, mesenchymal stem cells, embryonic stem cells, endodermal stem cells, ectodermal stem cells, trophoblastic stem cells, mesodermic stem cells, cardiomyoblastic stem cells, endocrine stem cells, neurogenic precursor cells, skin
- 25 precursor cells, renal precursor cells, hepatic precursor cells, pancreatic precursor cells and endothelial cells.
16. A method according to claim 15, whereby the stem or progenitor cells are human stem or progenitor cells.
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17. An Asb-a polypeptide having an amino acid sequence with at least 39% amino acid identity with SEQ ID NO: 1 or 3, and having the capability to suppress NGF-

induced terminal neuronal differentiation of PC12 cells, while allowing a conversion of the cells to a neuronal precursor state and allowing proliferation of the cells.

18. A nucleic acid molecule comprising a nucleotide sequence that encodes an Asb-a polypeptide having the capability to suppress NGF-induced terminal neuronal differentiation of PC12 cells, while allowing a conversion of the cells to a neuronal precursor state and allowing proliferation of the cells, whereby the nucleotide sequence is selected from the group consisting of:

- (a) a nucleotide sequence encoding a polypeptide comprising an amino acid sequence having at least 39% identity with the amino acid sequence of SEQ ID NO:1 or 3;
- (b) a nucleotide sequence that has at least 35% identity with a nucleotide sequence as depicted in SEQ ID NO:2 or 4;
- (c) a nucleotide sequence the complementary strand of which hybridises to a nucleotide sequence acid having a sequence as depicted in SEQ ID NO:2 or 4; and,
- (d) a nucleotide sequence which differs from the nucleotide sequence of (c) due to the degeneracy of the genetic code.

19. A vector comprising a nucleic acid molecule as defined in claims 18.

20. An expression vector comprising a nucleic acid molecule as defined in claim 18, wherein the nucleotide sequence encoding the Asb-a polypeptide is operably linked to a promoter capable of directing expression of the coding sequence in host cells for the vector.

21. An expression vector according to claim 20, wherein the promoter is a promoter that is active in stem or progenitor cells.

22. An expression vector according to claim 21, wherein the promoter is a promoter is a promoter selected from the group consisting of an Oct4 promoter, an Oct5 promoter, a TCF-regulated promoter, a LIF-regulated promoter, and a Notch IC/Her1-targeted promoter.

23. A host cell comprising a vector as defined in any one of claims 19 - 22.

24. A method for producing an Asb-a polypeptide, the method comprising the step of culturing a host cell as defined in claim 23 under conditions conducive to the expression of the polypeptide, and, optionally recovering the polypeptide.
- 5 25. A host cell according to claim 23, wherein the host cell is a stem or progenitor cell.
26. A stem or progenitor cell comprising an exogenous Asb-a polypeptide, an exogenous nucleotide sequence encoding an Asb-a polypeptide or both.
- 10 27. A stem or progenitor cell according to claim 26, whereby the stem or progenitor cells are selected from the group consisting of hematopoietic stem cells, neural crest stem cells, mesenchymal stem cells, embryonic stem cells, endodermal stem cells, ectodermal stem cells, trophoblastic stem cells, mesodermic stem cells,
- 15 cardiomyoblastic stem cells, endocrine stem cells, neurogenic precursor cells, skin precursor cells, renal precursor cells, hepatic precursor cells, pancreatic precursor cells and endothelial cells.
28. A pharmaceutical preparation comprising a stem or progenitor cell as defined in
- 20 claims 26 or 27.